



REVIEW OF HERBAL MEDICINE AS A NATURAL GIFT AND PROPER RIFLE TO OVERCOME PATHOGENIC INFECTIONS

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Review

ABSTRACT

Plants are used for several purposes in different industries like pharmacy, food, cosmetic etc. Some of them like spices have antimicrobial and antioxidant properties due to their capacity to produce secondary metabolites. In recent decade, the emergence of novel diseases, epidemics, and even pandemics along with the ability of a large group of pathogens to adapt against available antibiotics have caused scientists to explore natural and new sources of antimicrobial agents. These natural antimicrobial compounds are broadly used to design innovative drugs, in particular for those pathogenic strains that have been resistant to existing antibiotics in market. This review represents some of the recent findings on the antimicrobial activities of medicinal herbs.



Keywords: antibacterial potential, antibiotics, bacterial infections, medicinal plants, resistance

INTRODUCTION

The use of herbal drugs to treat a large number of diseases could be traced back to over 5 thousand years. Mankind started to explore components with acceptable therapeutic potentials as soon as they began to identify them (Nweze *et al.*, 2004; Vineela and Elizabeth, 2005; Pavithra *et al.*, 2010; Shinwari and Qaisar, 2011; Shakya and Shukla, 2011; Alzoreky and Nakahara, 2003; Clementi *et al.*, 2014; Zaheer *et al.*, 2021; Sultana *et al.*, 2021; Khouchlaa *et al.*, 2021). The term “medicinal herbs” refers to not only those used as sedative agents but also those that could be incorporated as flavors, drinks, sweeteners, natural pigments, herbicides as well as cosmetic products (Omidbeigi, 1997). Medicinal herbs are composed of adapted antimicrobial systems through production of secondary metabolites in their cells (Kim *et al.*, 1995; Ahmad and Beg, 2001; Alagesabopathi, 2011).

In folklore medicine, herbal drugs are used to mitigate the risks of pathogenic infections. Awareness of side effects involved in the application of chemical drugs might shift people’s interest towards more natural products to avoid such health issues. Beside side-effects, the incidence of multi resistant pathogenic strains to available antibiotics is considered to be another driving force towards finding a proper candidate to overcome resistant strains.

Developments in chemical sciences and the discovery of complicated synthetic organic systems have led to the outreach of pharmacology. On the basis of WHO report, it is estimated that 80 percent of population worldwide are positive towards medicinal herbs and conventional medication methods applied by folk healers. Plants used in such cases contain different constituents that allow them to be used as a part of food supplements, phyto-pharmaceuticals, novel drugs and many more (Farnsworth and Loub, 1983; Hammer *et al.*, 1999; Mukherjee, 2002; Janovska *et al.*, 2003; Bodeker *et al.*, 2005; Ahmed *et al.*, 2020).

From the economical viewpoint, plants are considered to be a proper revenue source due to their biologically active secondary metabolites such as phenolic compounds with different phyto-pharmaceutical activities (Stary and Hans, 1998). It is almost popularized the empirical application of medicinal plants and most countries have organized their facilities to contribute in screening programs of medicinal plants in order to explore and stabilize their antimicrobial activities in primary health care (Baba-mousa *et al.*, 1999). Like most organisms, medicinal herbs are influenced by environmental conditions that cause changes in appearance, flower, leaves, fruits, and in particular natural composition profiles

which can even alter the antimicrobial activities (Balandrin *et al.*, 1985). Currently, medicinal plants are collected either in small quantities for domestic purposes or in large scales by factories to valorize them by increasing the number of components that could be extracted and pharmaceutically employed (Bhowmik *et al.*, 2010).

Such compounds called phytochemicals are suggested as one of the disease-fighting strategies (Abu-Izneid *et al.*, 2020; Imran *et al.*, 2021). Phytochemicals are secondary metabolites produced by medicinal plants that can be prescribed directly to limit the microbial growth, or can be used as leading compounds against pathogenicity (Jahn *et al.*, 1986; Jabeen *et al.*, 2008).

The potentials of using herbal drugs as antimicrobial agents have drawn researchers’ attention recently, as reflected by the number of published studies on the introduction of superseded anti-microbial agents. The main scores involved in the application of herbal drugs might be their availability, affordability in production, being nonhazardous and environmentally friendly (Soldati, 1997; Martino *et al.*, 2002; Shahidi Bonjar *et al.*, 2004; Joseph *et al.*, 2008; Pitchai *et al.*, 2010).

Most plant-derived secondary metabolites screened by laboratory techniques, including in vitro methods, have been evaluated for possible antimicrobial activity, which in turn leads to providing a platform to make proper selection of crude extracts for further pharmacological researches (Mathekaga and Meyer, 1998; Alli smith, 2009). Table 1 summarizes some of the recently published literature on the application of medicinal herbs against pathogens.

Secondary metabolites are glycosides, saponins, flavonoids, steroids, tannins, alkaloids, terpenes and their potentials to combat divergent pathogenic microorganisms is outstanding (Davis, 1994; Lopez *et al.*, 2001; Anthara and Amla, 2012).

With no doubt, antibiotics are one of the most leading discoveries achieved in the 20th century. Nevertheless, less than half of infectious diseases are being medicated using them (Preethi *et al.*, 2010; Sharma, 2011). This might arise from the consecutive years of pathogenic outbreaks and their widespread along with successive and misuse of antibiotics. Therefore, the incidence of multi-drug resistant pathogenic strains shifting towards a global therapeutic issue (Dean and Burchard, 1996; Enne *et al.*, 2001; Westh *et al.*, 2004).

One major challenge that scientists face is how to control drug resistant pathogenic strains with less vulnerability to antibiotics. This has led to the exploration of innovative drug sources with lower side effects and reduction of

adulteration (Silver, 1993; Sieradzki *et al.*, 1999; Debasis, 2014). This review aims at presenting a perspective on previous and recently findings on the application of medicinal herbs to overcome infections caused by pathogens as a contribution towards introducing herbal drugs as an innovative solution to mitigate the incidence of resistant pathogenic strains.

Bioactive components derived from medicinal herbs

One characteristic discriminating plants as medicinal herbs is the metabolic mechanisms of secondary metabolite production as final products that can be applied to treat various maladies. Some of the natural secondary metabolites in medicinal herbs are presented in the next section.

Alkaloids

Alkaloids are defined as chemical compounds with at least one nitrogen atom in a heterocyclic ring. Biologically, alkaloids are nitrogen components produced through synthetic methods or found in naturally occurring forms in plants or animals. Most alkaloids are crystalized components which could combine with acids and produce mineral salts.

These components are explored either in free form, salts or N-oxides and mostly accumulated in storage tissues including roots, stems, flowers, seeds and active photosynthetic tissues. The production rate of alkaloids wane as the end of autumn approaches. The amount of alkaloids constitutes 10 percent of dry weight of epidermal tissues like cocaine, colchicine, as well as steroidal alkaloids like nicotine. The stated alkaloids are considered to be the first plant defending system.

The structure of alkaloids varies with respect to the synthesizing and accumulation location, the stage of growth, their life cycles, as well as plant sections. After addition of sodium bicarbonate and/or ammonium, alkaloids would be precipitated and extracted using organic solvents (Torras-Claveria *et al.*, 2014). Up to now, more than 5000 alkaloids have been detected in different parts of plants like pomegranate root, poppy capsule, datura leaves, and cannabis fruit. Interestingly, alkaloids have effects on nerve system and have sedative properties. They also have anti-cancer activities, stimulating impact like caffeine in coffee, and anti-parasite activity like alkaloids present in pomegranate root (Torras-claveria *et al.*, 2014). Figure 1 depicts some of the alkaloids.

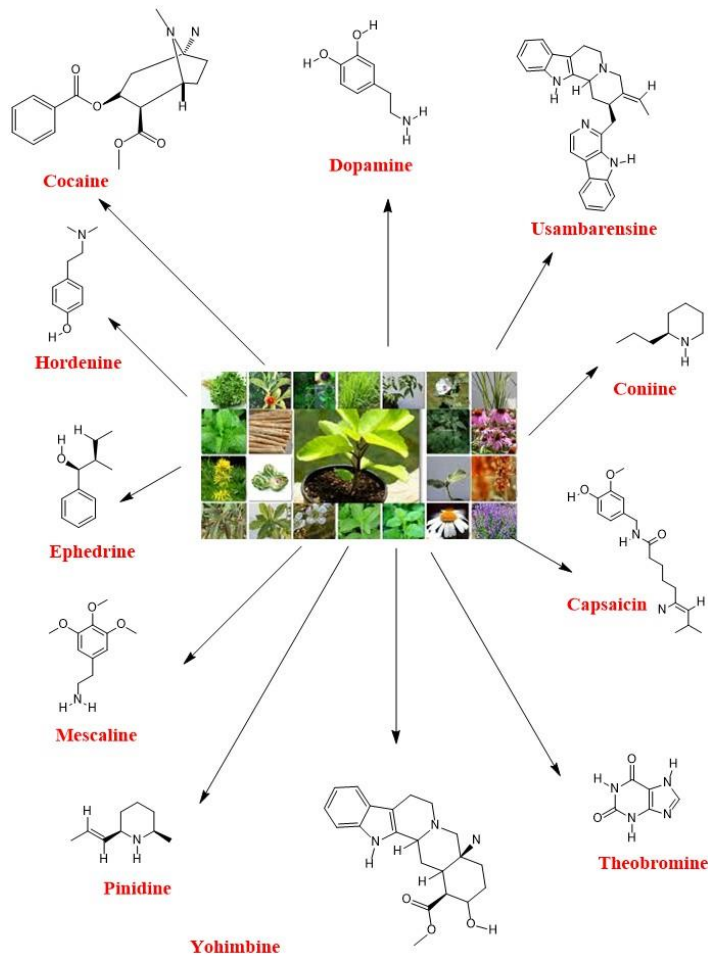


Figure 1 Selected alkaloids in medicinal herbs

Flavonoids

Flavonoids are plant-based compounds with heart healing properties. The term “flavonoids” represents a large group of phenolic compounds that are derived from phenyl propanoid with a-Fifteen-Carbonyl atom structure. These compounds carry out various functions in plants such as plant pigmentation and UV filtration in plants. They could also perform some functions in the human health care system; increasing antimicrobial strength, mitigating oxidation through chelating ions such as iron and copper, controlling cancer cells within gene expression, improving immune system, playing anti-viral, anti-inflammation, anti-allergic, and anti-mutation and even anti-hepatitis roles in the body (Kumar and Pandey, 2013).

Glycosides

Glycosides are secondary metabolites composed of a simple sugar like glucose which is linked to another functional compound by means of glycosidic bond. Glycoside are classified on the basis of glycone type, type of glycosidic bond as well as aglycone.

Bitter compounds

Pharmacologically, bitter components are related to terpenic group which leads to the release of azolene and other glycosides with different chemical structures (Aliani and Eskin, 2017).

Terpenes

Terpenes, the main constituents of essential oils, are built of carbohydrate. Some of the terpenes contain oxygen included components like alcohol, aldehyde or ketones, but are still categorized as terpenes. Various classifications of terpenes are as below (Breitmaier and Eberhard, 2006):

- Hemi-terpene: They are made of a unit of isoprene. Isoprene is considered merely to be a hemiterpene. However, some of the hemi-terpenes include oxygen like isovaleric acid.
- Mono-terpenes: composed of two units of isoprene. One of the alcoholic monoterpene is geranyl.
- Sesquiterpene: contains 3 units of isoprene like farnesyl.
- Diterpene: made of 4 units of isoprene and are derived from geranyl pyrophosphate.
- Sesterpene: made of 5 isoprene
- Triterpene: made of 6 units of isoprene. Squalene, the main part of isoprene of shark liver oil, is a member of this group.
- Tetraterpene: made of 8 units of isoprene such as no ring Lycopene
- Poly-terpene: made of a long chain of isoprene like natural rubber.

Essential Oils

Essential oils are recognized as liquid components at ambient temperature, solid at cold temperatures, and soluble in organic solvents like chloroform, acetone (Reddy, 2019). They contain different micro-constituents (Figure 2).

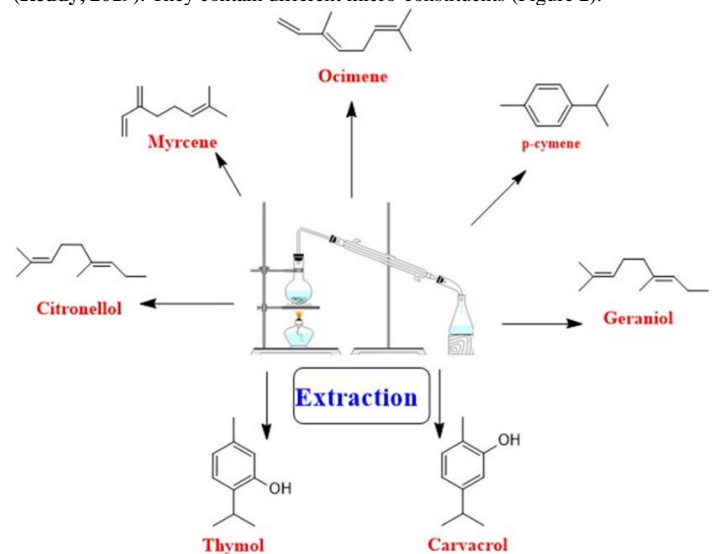


Figure 2 Selected micro-constituents that are presented in essential oils.

Antimicrobial properties of essences

Since essential oils have hydrophobic properties, they could easily diffuse in lipid membranes of bacteria or mitochondria, resulting in interference of efflux pump mechanism which causes the leakage of vital molecules and ions from bacteria,

ultimately leading to death (Cox et al., 2000). The same mechanisms also lead to death of fungi cells (Ultee and Smid, 2000). The position of hydroxyl group in essence determines how much antimicrobial activity might a compound depict. (Dorman and Deas, 2000).

Effective factors on antimicrobial activities of essential oils

There are several factor affecting antimicrobial activity of essential oils; they are categorized into 2 groups, internal or intrinsic properties of food such as structure, water content, protein, carbohydrate, salt and pH, and external factors including temperature, light, atmosphere and type of packaging (Tassou et al., 1995). Essential oils portray hydrophobicity which allow them to partition into membranes and therefore increase antimicrobial activity. Unlike fat and protein, carbohydrates have no protecting efficacy on bacteria (Mejlholm and Dalgaard, 2002). Physical structure of food has significant effect on antimicrobial activity. Thus essential oils are more effective against pathogens in liquid food media such as milk, compared to solid structures like meat (Skandamis et al., 2000).

Mechanisms of action

Antimicrobial activity of extracted compounds has been evaluated individually in laboratories. However, the obtained results from various studies have been contradictory and this makes their comparing and judgement effortful (Mann and Makham, 1998; Manou et al., 1998; Skandamis et al., 2001). Besides, it is not still clarified whether the applied methods are targeting to evaluate antimicrobial activity and/or to mitigate the microbial growth. Antimicrobial assessments measure the diameter of inhibited growth area around inoculated paper-discs with an antimicrobial compound on agar considering the following: inhibition of bacterial growth on agar surface with diffused antimicrobial components; and minimum inhibition concentration of antimicrobial activity in liquid environment.

In addition, three important factors which might influence the results of experiments are:

- the combination of parameters in regard to test samples;
- the type of microorganisms and their growth conditions;
- the applied methods in counting of live bacteria.

Most studies like diffusion disc or turbidimetry are on the basis of growth inhibition. The uniform distribution of essential oils in agar is of great importance. Besides uniformity, the present of bioactive compounds are also effective on the results; in lower concentrations, bioactive compounds could act in antagonistic or synergistic manner.

Diversity in the antimicrobial reactions of the components arise from their simple form or their use in combination with complexes (Stechini et al., 1993, 1998). Considering the type of reaction, various determination methods are used. Turbidimetry is a non-destructive and inexpensive method but has low sensitivity. This method could help with determination of upper section of growth curve; therefore, to correlate the results with the counting of live cells in agar, the method needs to be calibrated.

Changes in absorbance manifest the only response when the total count is 10⁶-10⁷ CFU/ml. The physiological conditions of cells (intact or destroyed), and oxidation level of essential oils could be effective on the absorbance level. Despite total count techniques, impedance methods are based on monitoring of microbial metabolism. Impedance techniques are employed to screen destroying activities and to assess growth kinetics in mathematical models (Lachowicz et al., 1998).

Conventional techniques depend on the number of live cells counted in plates. However, such techniques are time-consuming and require high-costs. Minimum inhibition concentration (MIC) is determined through consecutive dilution of broth by plate count (Lambert and Pearson, 2000). This requires increasing the monitoring of compounds and microorganisms (Lambert and Pearson, 2000). It could favor simultaneous evaluation of single or several preservatives, and consequently determination of MIC based on mathematical models.

Food applications

Microorganisms are considered to be one of the oldest and successful creatures in our planet, due to their high adapting and survival potentials compared to other organisms that are annihilated after a while. Subjecting pathogenic microbes to antibiotics produced from other microorganisms (the latter introduced as probiotics) could lead to the development of resistant mechanism; therefore, it is not surprising that mankind encourages the ever growing problematic challenges in regards to the control of microbes (Opal et al., 2000).

It is estimated that 10-20 percent of plant population could be used as drugs to serve health care processes like isolation, purification and extraction of herbal drugs which may lead to the production of a group of components with biological activities (Nacz and Shahidi, 2006; Kibwage et al., 2006).

Among the extracted components, some of them like essential oils have antimicrobial activity. In-vivo techniques are used to evaluate antimicrobial activities of essential oils (Nychas and Tassou, 2000). Some of the ambient conditions are also critical for the efficacy of antimicrobial lethality like the

presence of oxygen. For instance, Paster and coworkers found that essential oil of thyme is active against *S. aureus* and *S. enteritidis* in aerobic and anaerobic conditions (Paster et al., 1990). In addition, essential oil of oregano was more effective in the presence of 41% CO₂, 31% oxygen, and 31% nitrogen compared to air permeable packs. In another study, essential oil of oregano was shown to have antimicrobial activity against *S. aureus* and *S. enteritidis* at modified atmosphere packaging at 1°C, and *S. putrefaciens* and *P. phosphurum* in treated cod fish with essential oil of oregano (Tassou, 2002).

Essential oils are mostly combined with protein, fat, sugar and salt, therefore only a low concentration of essential oil (EO) which remains free could exhibit antimicrobial activity. External factors like temperature limit antimicrobial activity of EO (Davidson, 1997). Physiological properties of bacteria grown in food matrices differ remarkably from those grown in different liquid cultures. Such differences could be due to the following reasons: population, availability of nutrients, availability of oxygen, and the accumulation in final products.

Mechanism of action

The mechanism of action of essential oils depends on the concentration (Prindle and Wright, 1977). Lower concentrations prevent energy related enzymes while higher amounts cause precipitation of proteins. Nonetheless, it is still under question whether the damages to membranes are associated with the amount of antimicrobial compounds contacting the cell membrane or their effects on cell injuries leading to cell death. Solutions of trace elements like iron have negative effects on essential oils. Hence, one proper way to inhibit microbial growth might be limitation of cell availability to such ions like irons. Furthermore, ferrous ion could combine with phenolic compounds and indirectly lead to cell destruction owing to oxidative stress (Friedman and smith, 1984). Aldehyde groups in some animal and plant tissues react with main base and prevent biosynthesis of the cell wall (Patte, 1996). Phenolic compounds, essential oils and phytoalexin are mostly active to inhibit microbial growth, rather than exhibition of toxic effects (Tokutake et al., 1992). Leakage of cell membrane might not directly inhibit microbial growth, but decelerate the metabolic processes of meiosis (Kubo et al., 1985). Behavior of essential oils in destroying gram positive or gram negative bacterial could be considered as another critical reason.

Compared to gram negative bacteria, gram positive ones are more sensitive (Dabbah et al., 1970; Shelef et al., 1980, 1983; Farag et al., 1989), yet various inhibiting mechanisms could be found among gram negative bacteria. For instance, *E. coli* is more resistance than *S. flurescence* or *C. marcescense* when exposed to essential oils of rosemary, garlic and thyme (Farag et al., 1989). Mutated *E. coli* and *S. aureus* are resistant against essential oils of pine (Moken et al., 1997).

In recent times, scientific results have shown that pharmaceutically extracted compounds belong to phenolic compounds, vitamins and tannins with striking antioxidant activity (Suffredini et al., 2004). Many papers have been published on the basis of the possible antimicrobial activities of medicinal herbs against gram positive and gram negative bacteria (Evans et al., 2002). Both negative and positive gram bacteria could be responsible for various ailments. For instance, gram (+) bacteria like *Staphylococcus aureus* could create wound infection, toxic shock syndrome and food poisoning (Benayache et al., 2001) while gram (-) bacteria like *E. coli* is the main reason of diarrhea in human, and also can cause coleocystis or septicaemia (Benhassaini et al., 2003). Among recently detected infections, those caused by Methicillin-resistant *Staphylococcus aureus* (MRSA) are of great importance owing to their high adaptability in overcoming almost all clinically antibiotics available in the market (Adwan et al., 2009). As previously stated, a problematic issue in destroying the pathogens might be their adaptability to antibiotics and application of herbal medicine might be a superior candidate to control them.

Pathogens employ various mechanisms to control antibiotics like specialized efflux systems. One of the other pathogen that is resistant to different available antibiotics, *P. aeruginosa* enjoys the mentioned strategy to overcome antibiotics (Elbashiti et al., 2011). Another mechanism to protect pathogens against antibiotics is the production of extended-spectrum β Lactamases-M (ESBLs) enzymes (Darwish and Aburjai, 2010).

CONCLUSION

Generated flavors through application of essential oils, presence of the aromatic components in medicinal herbs together with necessities to high-cost methods in order to find antimicrobial agents among bioactive components have limited the use of essential oils as antimicrobial agents. Application of such compounds should be under an accurate selection system along with evaluation of their antimicrobial potentials in the least concentrations. Incorporation of essential oils to food formulae or using them, either alone, in combination with other chemical preservatives, could favor their synergistic effects in fighting against various infections and spoilage. The prospect of synergistic effect of the simultaneous application of various spices and medicinal herbs in designing new drugs and replacing chemical drugs with such sources would be of great importance in future research studies.

Table 1 Some recently published studies on the application of herbal drugs in fighting against pathogens

| Name | Used section | Used solvent or extraction technique | Targeted Microorganism | Ref |
|---|---|---|---|--------------------------------------|
| <i>Ballota bullata</i> Pomel | essential oil aerial parts | Hydro distillation | <i>E. coli</i> , <i>P. aeruginosa</i> , <i>S. enterica</i> , <i>S. aureus</i> , <i>B. subtilis</i> , <i>C. albicans</i> | El mokni et al., 2020 |
| <i>Nicotianatabacum L.</i> | Roots | hexane | <i>S. aureus</i> , <i>E. coli</i> , <i>P. aeruginosa</i> , <i>C. albicans</i> and <i>E. floccosum</i> | Al-lahham et al., 2020 |
| <i>Nicotianatabacum L.</i> | Roots | acetone | <i>S. aureus</i> , MRSA, <i>E. faecium</i> , <i>E. coli</i> , <i>S. sonnie</i> , <i>P. aeruginosa</i> , <i>C. albicans</i> and <i>E. floccosum</i> | Al-lahham et al., 2020 |
| <i>Nicotianatabacum L.</i> | Roots | methanol, | <i>E. faecium</i> , <i>E. coli</i> , <i>S. sonnie</i> <i>C. albicans</i> | Al-lahham et al., 2020 |
| <i>Curcuma caesia</i> Roxb. | essential oil of leaves | Hydrodistillation | <i>B. subtilis</i> , <i>B. cereus</i> , <i>S. aureus</i> , <i>S. typhimurium</i> , <i>A. fumigatus</i> , <i>A. niger</i> , <i>S. cerevisiae</i> , <i>C. albicans</i> . <i>E. coli</i> ATCC | Borah et al., 2019 |
| <i>Satureja montana</i> | byproducts essential oils | Hydro distillation technique | 25922, <i>S. enterica</i> sv Anatum SF2, <i>S. aureus</i> ATCC 6538 | Santos et al., 2019 |
| <i>T. foliolosum</i> | leaves | methanol, chloroform, hexane and aqueous | <i>A. tumefaciens</i> , <i>B. subtilis</i> , <i>E. chrysanthemi</i> , <i>E.</i> <i>coli</i> , <i>X. phaseol</i> | Joshi and Sati (2014). |
| <i>Parkia biglobosa</i> | seeds | chloroform | <i>C. albican</i> , <i>A. fumigatus</i> , <i>C. neoformans</i> , <i>E.</i> <i>coli</i> , <i>P. aeruginosa</i> , <i>K. pneumoniae</i> , <i>V. resistance</i> <i>enterococcus</i> , MRSA | Bello et al., 2018 |
| <i>Leptadenia hastata</i> | leaves | methanol | <i>C. albican</i> , <i>A. fumigatus</i> , <i>C. neoformans</i> , <i>E.</i> <i>coli</i> , <i>P. aeruginosa</i> , <i>K. pneumoniae</i> , <i>V. resistance</i> <i>enterococcus</i> , MRSA | Beloo et al., 2018 |
| <i>Zanthoxylum zanthoxyloides</i> and <i>Gongronema latifolium</i> | | ethyl acetate, chloroform | <i>E. coli</i> , <i>P. aeruginosa</i> , <i>Klebsiella sp.</i> , <i>S.</i> <i>pneumoniae</i> <i>B.</i> <i>cereus</i> , <i>A. niger</i> , <i>A. flavus</i> , <i>Trichoderma sp.</i> , <i>Candida sp</i> | Adeeyo et al., 2020 |
| <i>Nauclea latifolia</i> Smith. | Whole fruit | n-hexane, ethylacetate, n-butanol | <i>S. aureus</i> , <i>S. sonnei</i> | Oyedjeji-Amusa and Ashafa, 2019 |
| <i>F. deltoidea</i> | leaves | Chloroform, methanol | <i>S.aureus</i> | Ashraf et al., 2019 |
| <i>Orthosiphon stamineus</i> , | leaves | methanol chloroform, | MRSA | Ashraf et al., 2019 |
| <i>Pittosporum angustifolium</i> Lodd. | Leaves | methanolic, aqueous, ethyl acetate | <i>P. mirabilis</i> , <i>K. pneumonia</i> | Blonk and Cock, 2019 |
| <i>Dictamnus dasycarpus</i> Turcz. | Aerial part Essential oil | Hydro distillation | <i>C. albicans</i> | Tian et al., 2019 |
| <i>Persicaria pensylvanica</i> | flower, leaf, stem and root | methanol | MRSA | Abdi and Dego, 2019 |
| <i>Eleaegnus indica.</i> | Aerial parts | Acetone, hexane | <i>M. racemosus</i> | Srinivasana et al., 2019 |
| <i>Eleaegnus indica.</i> | Aerial parts | ethyl acetate | <i>E. faecalis</i> | Srinivasana et al., 2019 |
| <i>Eleaegnus indica.</i> | aerial parts | Methanol | <i>S. epidermidis</i> , <i>S. pneumoniae</i> | Srinivasana et al., 2019 |
| <i>Amaranthus spinosus</i> | | ethanolic | <i>S. epidermidis</i> , <i>S. typhi</i> , <i>S. typhimurium</i> <i>C. krusei</i> , <i>A. fumigatus</i> | Paswan et al., 2019 |
| <i>L. angustifolia</i> , <i>C. citratus</i> and <i>M.</i> <i>piperita</i> | Leaves | Ethanol extract | <i>S. aureus</i> , <i>E. coli</i> and <i>C. albicans</i> | Gishen et al., 2020 |
| <i>Citrus sinensis</i> | seed oil | n-hexane, methanol | <i>anit-toxoplasma gondii</i> | Atolani et al., 2020 |
| <i>P. amarus</i> | Leaves | ethanolic extract | <i>S. marcescens</i> , <i>E. coli</i> , <i>S. typhimurium</i> , <i>P.</i> <i>aeruginosa</i> , <i>C. albicans</i> | Maria Braga Ribeiroa et al., 2019 |
| <i>Aerva lanata</i> | whole plant | Chloroform Hexane Ethyl acetate Water methanol | <i>E. coli</i> , <i>E. aerogenes</i> | Al-ansari et al., 2019 |
| <i>Rubus fruticosus</i> Ldried | leaves | Methanol, hexane, ethyl acetate, Hydro alcoholic, Chloroform | <i>E. faecalis</i> , <i>S. aureus</i> , <i>E. coli</i> , <i>H. influenza</i> | Welia et al., 2020 |
| <i>Achillea cucullata</i> | aerial parts | Ethanolic extraction | <i>S.Aureus</i> , <i>E. faecalis</i> , <i>P. aeruginosa</i> , <i>E. coli</i> , <i>C.</i> <i>albicans</i> | Eruygur et al., 2018 |
| <i>Lepidium sativum</i> | seed oil | | <i>S. aureus</i> , <i>B. subtilis</i> , <i>E. coli</i> , <i>P. aeruginosa</i> , <i>S.</i> <i>enterica</i> , <i>K. pneumoniae</i> , <i>C. albicans</i> <i>B. cereus</i> , <i>E. faecalis</i> , <i>E. faecium</i> , <i>E.coli</i> , (MRSA) <i>S. typhimurium</i> , <i>V. parahaemolyticus</i> , <i>Y.</i> <i>enterocolitica</i> , <i>Y. pseudotuberculosis</i> , <i>C. albicans</i> | Alqahtani et al., 2018 |
| <i>Centaurea hypoleuca</i> | stem | Ethyl acetate | | Ozcan et al., 2019 |
| <i>Centaurea hypoleuca</i> | Ethyl acetate, methanol flower | | <i>C. albicans</i> | Ozcan et al., 2019 |
| <i>Centaurea hypoleuca</i> | Methanol Ethyl acetate flower , stem | | <i>C. albicans</i> | Ozcan et al., 2019 |

| | | | | |
|--|--------------------------------------|--------------------------------|---|---|
| <i>Centaurea hypoleuca</i> | Methanol Ethyl acetate flower , stem | | <i>V. parahaemolyticus</i> | Ozcan et al., 2019 |
| <i>Centaurea hypoleuca</i> | Flower | Ethanol Methanol Ethyl acetate | <i>B. cereus</i> | Ozcan et al., 2019 |
| <i>Hydnora abyssinia A.Br.</i> | Root | Ethanol | <i>E. coli, S. typhimurium, and S. aureus.</i> | Guadie et al., 2020 |
| <i>Hydnora abyssinia A.Br.</i> | Root | aqueous | <i>E. coli, S. typhimurium</i> | Guadie et al., 2020 |
| <i>Hydnora abyssinia A.Br.</i> | Root | acetone | <i>E. feacalis, E. coli, S. typhimurium</i> | Guadie et al., 2020 |
| <i>Leucas aspera (Willd.)</i> | Leaves | ethanol | <i>E. coli, E. feacalis and S. aureus</i> | Guadie et al., 2020 |
| <i>Solanum incanum L.</i> | Root | | <i>E. coli, E. feacalis and S. typhimurium</i> | Guadie et al., 2020 |
| <i>Harrisonia abyssinica Oliv.)</i> | Stem | Ethyle acetate | <i>E. coli, S. typhimurium, S. aureus</i> | Guadie et al., 2020 |
| <i>Harrisonia abyssinica Oliv.)</i> | Stem | Ethanol extract | <i>E. feacalis, E. coli, S. typhimurium, S. aureus.</i> | Guadie et al., 2020 |
| <i>Veronicastrum latifolium (V. latifolium)</i> plant oils; Tea tree, Cinnamon, Rosemary, Cactus, Lavender, Basil, Lemon, Thyme, Parsley, Almond and Lupine. <i>Foeniculum vulgare Mill.</i> Black pepper | | | <i>S. aureus, B. subtilis. E. coli, P. aeruginosa, A. baumannii, C. albicans</i> | Yin et al., 2019 |
| | | | <i>S. aureu, S. epidermidis, C. acnes</i> | Esmaeil et al., 2019 |
| | | | <i>C. albicans, B. cereus S. aureus, B. cereus, and S. faecalis</i> | Ilić et al., 2019 Shityakov et al., 2019 |
| <i>Melissa officinalis</i> | Essential oil of aerial part | Water-distillation | <i>Botrytis cinerea, Penicillium expansum and Rhizopus stolonifer. Erwinia, S. aureus, C. violaceum, carotovora, B. subtilis, P. aeruginosa and E. coli, C. violaceum</i> | El Ouadi et al., 2017 |
| <i>Rosa damascena:</i> | | | | Akram et al., 2019 |
| <i>Rumex species-</i> | | | Antimicrobial activity | Prakash Mishra et al., 2018 |
| <i>Habanero Chili</i> | | | <i>Salmonella enterica subsp. Typhimurium (33 %) and Yersinia enterocolitica(16.65 %).</i> | Hleba et al., 2015 |
| Pollen | | | Antimicrobial activity | Kostic et al., 2020 |
| <i>Hypoxis hemerocallidea</i> | | | Anti-HIV | Laila et al., 2019 |
| <i>Artemisia annua L</i> | | | Anti-HIV activity | Laila et al., 2019 |
| Pomegranate | | | <i>M. R. S. aureus S. entrididis L. monocytogenese Paeroginosa E coli</i> | Pirzadeh et al., 2020 |
| <i>Diospyros lotus</i> | Roots | Methanolic | <i>E. coli, S.aureus, B. subtilis, K. pneumonia S. epidermis</i> | Rauf et al., 2020 |

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